REMARKS

Claims 3-4, 6 and 10-25 presently appear in this case. No claims have been allowed, although it is noted that claims 4, 10, 13, 14, 15, 16, 17, 18, 21 and 22 have only been been "rejected because they are dependent upon rejected claims". The Official Action of December 17, 2003, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to the use of Compound B combined with human growth factors in promoting angiogenesis. Such a combination can be used as cicatrizants to treat wounds, ulcers and other traumatic lesions. The combination of Compound B and human growth factor has a synergistic effect.

Claims 19 and 23 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite in the use of the term "relative amount". The examiner states that it is not clear what is that amount which would provide synergistic results and relative to what.

Claims 19 and 23 have now been amended to delete the term "relative amount". The claim now refers to the ratio of the amount of Component B to the amount of human growth factor. This language is very clear and definite. The amount

of the ratio is defined functionally as being that amount which is effective to provide synergistic angiogenesis results. It should be noted that MPEP §2173.05(g) states:

> There is nothing inherently wrong with defining some part of an invention in functional terms. Functional language does not, in and of itself, render a claim improper.

See also *In re Watson,* 186 USPQ 11, 20 (CCPA 1975), where it states:

> Moreover, the claim language must be read in light of the application disclosure as it would be interpreted by one of ordinary skill in the art. ... Those skilled in the art will be able to determine from the disclosure, including the examples, what an effective amount of germicide is. ... In the context of the claimed subject matter, the disputed phrase reasonable defines the metes and bounds of the invention to one of ordinary skill in the art.

Accordingly, it is believed that the new claim language of claims 19 and 23 fully comply with the second paragraph of 35 U.S.C. §112. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

Claims 3, 6, 11, 12, 19, 20 and 23-25 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Martelli taken with Folkman. The examiner states that Martelli discloses a pharmaceutical composition comprising Component B as active ingredient, together with a pharmaceutically acceptable carrier for the treatment of wounds, ulcers and other traumatic lesions. The examiner

states that Folkman teaches several angiogenic proteins whose angiogenic activity can be synergistic. The examiner concludes that in view of the fact that Martelli teaches Component B in a composition, it would have been obvious to one of skill in the art to have combined Martelli's Component B with Folkman's angiogenic protein to give synergistic results. This rejection is respectfully traversed.

First of all, with respect to claim 11, which is directed to a method of promoting angiogenesis, there is nothing in Martelli that would teach or disclose this utility. Martelli does not teach or suggest that Component B can be used as an angiogenic agent, nor does it teach or suggest use of Component B together with human growth factors for causing angiogenesis. While Folkman teaches that two human growth factors can act synergistically with one another, this would in no way teach or suggest that Component B has angiogenic activity, nor would it teach or suggest that a human growth factor can act synergistically with Component B.

With respect to claim 20, and those claims dependent therefrom, Martelli mentions the use of Component B as anti-inflammatory, anticoagulant, antitumorigenic, and cicatrizant for the treatment of wounds, ulcers and other traumatic lesions of the body. There is no teaching or suggestion that Component B has angiogenic properties. Folkman teaches that two growth factors have synergistic angiogenic effects when

combined with one another, as compared to the use of each alone. As the references teach different effects, it would not be obvious to combine them.

Furthermore, any *prima facie* case of obviousness for combining the two references would be overcome by the proof of unexpected results shown in the present specification. Reference is made to Figures 4A and 4B of the present application. In Figure 4A it can be seen that the angiogenic score over time for 500 ng of Component B (CB) alone and for 100 ng basic fibroblast growth factor (bFGF) alone can be seen. In Figure 4B, one can see the angiogenic score for 500 ng of CB administered with 100 ng bFGF. The angiogenic score when the two compounds are administered together (e.g., 4.8 on day 7) is clearly more than the sum of the angiogenic scores when the two compounds were administered separately (1 for bFGF and 1.2 for CB on day 7; sum equals 2.2).

In Table 3, the synergistic effect between Component B and vascular endothelial growth factor (vEGF) can be seen. When 500 ng CB is used alone, one out of five implants was scored as positive. When 100 ng of vEGF was used alone, one out of four implants was scored as positive. In contrast, when 400 ng of CB was used in conjunction with 100 ng of vEGF, four out of four implants were scored as positive. Clearly the two compounds work synergistically, in that the effect of

the two together is greater than the sum of their separate effects.

Accordingly, even if the examiner has established a *prima facie* case of obviousness (and it is not believed that the examiner has done this for the reasons discussed above), this *prima facie* case of obviousness has been rebutted by the showing of synergistic results presented in the present specification. The examiner states that Folkman teaches that synergism would be expected. However, Folkman only teaches that when bFGF and vEGF are used together they provide synergistic results as compared to the use of either one separately. There is no suggestion that the use of either of these will provide synergistic angiogenic effects if combined with Compound B, particularly since there is no prior art that discloses that Compound B has angiogenic effects at all. Reconsideration and withdrawal of this rejection are, therefore, respectfully urged.

The examiner states that claims 4, 10, 13, 14, 15, 16, 17, 18, 21 and 22 are rejected because they are dependent on rejected claims. This rejection is respectfully traversed.

The examiner's attention is invited to MPEP §608.01(n)V, where it states:

> If the base claim is rejected, the dependent claim should be objected to rather than rejected, if it is otherwise allowable.

See also MPEP 706.01. The examiner has not stated any independent ground for rejection of any of claims 4, 10, 13, 14, 15, 16, 17, 18, 21 and 22. The examiner has not taken the position that any of these claims would have been obvious from any of the references of record. Therefore, it is apparent that, other than the fact that they are dependent from a rejected claim, they would be allowable. Thus, the claims should be objected to rather than rejected, and the applicant should be informed that the examiner considers the claims otherwise allowable. That way the applicant could have the option of rewriting the claims in independent form, including all of the limitations of the base claim and any intervening claims, secure in the knowledge that doing so would place that claim into condition for allowance.

It is submitted that all of the claims now presented in the case fully define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,
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